

REMARKS

Claims Under Examination and Amendment of Claims 18 and 24

All of claims 18-62 are currently under examination. (Office Action of April 7, 2006, at page 1, Office Action summary.) Claim 18 is amended herein to remove part (b) reciting "amino acids" and to re-number the remaining sub-parts accordingly. Claim 24 is amended to recite "further comprising" the recited ingredients rather than merely "comprising." That simple amendment does not introduce either new matter or new search issues, and can be immediately entered. Further, it simplifies the issues should appeal be requested in future.

Thus, Applicants respectfully request the Office to enter the Amendment under 37 C.F.R. § 1.116.

All of the Claims are Definite Under 35 U.S.C. § 112, Second Paragraph

First, the Office rejects all of the pending claims under 35 U.S.C. § 112, second paragraph, asserting that independent claims 18, 33, and 48 are indefinite. (Office Action at page 3.) Applicants traverse that rejection because the claims are clear on their face.

Claims 18, 33, and 48 recite a "composition" comprising, *inter alia*, (1) a pure form of one or more specifically recited protease and/or precursor proteins, and (2) one or more other "substances" chosen from the list in parts (a) through (j) of claim 18 or (a) through (k) of claims 33 and 48. Among those additional "substances" are "amino acids," recited in claims 33 and 48, as well as, for example, "sugars," "detergents," "protease inhibitors," and others. The Examiner seems confused as to whether the

recited "amino acids" are part of the amino acid sequence of the claimed protease or precursor proteins in the composition or are different components added separately to the overall composition. (Office Action at page 3.)

The grammatical structure of the claims alone should settle the Examiner's confusion on this point. The claims clearly set forth that the recited "amino acids," like the other recited substances, are added to the composition as a whole. Indeed, if the "amino acids" were merely a part of the sequence of the recited protease and/or precursor proteins, it would be redundant to list them as separate ingredients. Moreover, when the Applicants wish to describe particular elements that are part of the protein sequences, those elements are specifically recited as comprising part of those sequences and not as part of the composition as a whole. (See the final clause of each claim beginning "wherein the amino acid sequence of the protease comprises the following . . .")

Definiteness is considered from the point of view of one of ordinary skill in the art reviewing the application taken as a whole. M.P.E.P. § 2173. Those in the art would recognize from the context of parts (a) through (k) of the claims that those parts are listing ingredients that are added to the composition separately from the protease and/or precursor protein. In addition, the specification as a whole describes them similarly as additional ingredients present in the composition as a whole. (See pages 5-6, for example.) For all of those reasons, all of the pending claims are definite.

Therefore, Applicants request the Office to withdraw this rejection.

Claims 18, 22, 24, 27, and 32 Are Novel

First, the Office rejects claims 18, 22, 24, 27, and 32 as allegedly anticipated by Choi-Miura et al. (*J. Biochem.* 119: 1157-1165 (1996); "Choi-Miura"). (Office Action at pages 4-5.) Applicants respectfully traverse that rejection.

To establish a *prima facie* case of anticipation, the cited reference must teach each and every limitation of the claim either expressly or inherently. M.P.E.P. § 2131. Further, in order to establish inherent anticipation, the Office "must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." M.P.E.P. § 2112, emphasis in original.

Choi-Miura describes the extraction from human plasma aliquots of a protein that its authors call PHBP, and a partial sequence characterization of that protein. But Choi-Miura does not describe the subject matter of claim 18, 22, 24, 27, or 32, which require a pure form of Applicants' claimed protease in a specific composition that comprises one or more of the expressly recited additional ingredients (a)-(j) presented in claim 18. For example, while Choi-Miura does mention eluting PHBP in 2M glycine-HCl buffer, it does not teach a composition "comprising the pure form of the protease activating blood clotting factor VII and one or more substances chosen from: complexing agents of divalent ions, sugars, detergents, alcohols, albumin, gelatin, fibronectin, vitronectin, reductants, and protease inhibitors." (See claim 18; see Choi-Miura at 1161, left-hand column.)

Moreover, the Office's reasoning for rejecting claims 22, 24, and 27 is that, for example, "PHBP contains arginine and cysteines." (Office Action at page 5, first two

lines.) Apparently the Office interprets the claims to mean that the "arginine" or the "cysteine" is in the protein's sequence, and is not a separately added ingredient in the composition as a whole. As stated above, that interpretation of the claims is not supported by the claim language.

For those reasons, Applicants request the withdrawal of this rejection.

Claims 18-24 and 27-32 are Nonobvious

The Office also rejects claims 18-24 and 27-32 as allegedly obvious in light of Choi-Miura in combination with Turner et al. (U.S. Patent No. 5,326,558). (Office Action at pages 6-7.)

A *prima facie* case of obviousness has three general requirements. M.P.E.P. § 2143. First, the combination of publications taken as a whole must teach or suggest all of the claim limitations. M.P.E.P. § 2143.03. Second, there must be a motivation to combine the teachings of the cited publications to obtain the invention as claimed. M.P.E.P. § 2143.01. Third, there must be a reasonable expectation of success in performing that combination. M.P.E.P. § 2143.02. Both the motivation to combine and the reasonable expectation of success must come from the prior art, assuming no knowledge of the applicant's invention. They cannot be derived from hindsight from the applicant's specification. M.P.E.P. § 2143.

In rejecting claims 18-24 and 27-32, the Office first contends that Choi-Miura teaches albumin as an extra ingredient because it was found as a contaminant of Choi-Miura's initial PHBP preparation. (Office Action at page 6, citing Choi-Miura at page 1158, last sentence of the second paragraph.) But, by definition, a "contaminant" is a

substance that is unwanted in a composition and that one desires to remove from, not to add to, the composition. Indeed, what Choi-Miura states is that “[t]he contaminating IgM and albumin in the PHBP preparation were removed by passage through columns of anti-IgG antibody-conjugated Sepharose and anti-albumin antibody-conjugated Sepharose, respectively, as described previously.” (*Id.*) Thus, Choi-Miura does not suggest adding albumin. It suggests removing albumin. Further, Turner makes no mention of albumin. Thus there is no motivation in Choi-Miura and Turner to include albumin in the claimed composition comprising a pure form of the protease activating blood clotting factor VII.

Second, the Office contends that while Choi-Miura does not teach “complexing agents of divalent ions” or “protease inhibitors” or “reductants” for example, Choi-Miura allegedly suggests that pure PHBP is susceptible to proteolytic cleavage. (Office Action at page 7.) The Office relies upon Turner for a suggestion of those agents, citing Turner at column 13, first incomplete paragraph. (*Id.*) However, there is no motivation to combine Turner and Choi-Miura in such a fashion.

First, Turner explains that the cocktail of protease inhibitors is added to extracted urine samples, which one would expect to contain many different types of harmful contaminants. (Turner at cols. 12-13.) Turner does not suggest adding that cocktail to a pure protein solution devoid of the contaminants from the urine. Further, the Office asserts that “Choi-Miura et al. have discussed that purified PHBP is susceptible to cleavage by proteolytic enzymes,” citing page 1162 of Choi-Miura. But Applicants fail to see where such susceptibility in a pure solution is discussed, either at that page or at any other page of Choi-Miura. What the paper does discuss is that PHBP, like many

mammalian proteins, seems to be cleaved from a longer precursor *in vivo*, and may itself have some type of serine protease activity. (See the paragraph bridging pages 1162-1163 of Choi-Miura.) But those properties have no relevance to the question of whether or not one should add a protease inhibitor to a pure solution of PHBP.

Thus, Applicants can find no suggestion in Choi-Miura that PHBP in pure form is somehow unstable to proteases. Nor is there a suggestion in Turner that one should add protease inhibitors to pure forms of proteins. Consequently, there is no motivation to combine those two publications so as to obtain claim 18 or any of Applicants' other claims.

Applicants therefore request the withdrawal of the obviousness rejections.

Provisional Obviousness-Type Double Patenting Rejections

Finally, the Office provisionally rejects several claims under the judicial doctrine of obviousness-type double patenting over claims from two co-pending applications: claim 13 of Application No 10/254,662 and claim 31 of Application No. 11/118,396. (Office Action at pages 7-11.)

Applicants note that Application No. 10/254,662 is now abandoned. Thus, the rejection is moot as to that application.

The 11/118,396 application is currently pending and under examination. Applicants acknowledge the rejection of claims 18-22, 24-26, 30-37, 39-41, "45-4-52," 54-56, and 60-62 as to that application and will consider whether or not a terminal disclaimer should be filed at the appropriate time. (Applicants are unsure whether "45-4-52" was intended to be claims 45-52 or another set of claims.)

Conclusion

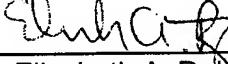
In view of the foregoing remarks, Applicants submit that this claimed invention, as amended, is in condition for immediate allowance, subject to considering the provisional obviousness-type double patenting rejection above. Should the Examiner have any questions about the amendments or remarks, he is invited to contact Applicants' representative.

Please grant any extensions of time required to enter this response and charge any required fees not otherwise found herewith to our deposit account 06-0916.

Respectfully submitted,

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Dated: July 7, 2006

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